

## REMARKS

In this response to the Final Office Action dated June 22, 2009, Claims 1 and 12 have been amended to correct informalities and further specify the subject matter. Support for the amendment to Claim 1 can be found, for example, from paragraphs [0021] and [0022] of the published application. The amended Claim 12 is supported by the original Claim 15, which is now incorporated into Claim 12 and canceled without prejudice. As such, the amendments in this response do not add any new matter. Currently, Claims 1, 3-6, 8-14, 16, and 19-25 remain pending and Claims 1, 3-6, 8-16, 24, and 25 are presented for the Examiner's consideration.

By these amendments and remarks as set forth herein, withdrawal of the rejections and reconsideration of the Claims are respectfully requested.

### **Objection of Claims 1 and 12**

The Examiner objected to Claims 1 and 12 as the term "capable of" in the claims is allegedly indefinite. In reply, Claims 1 and 12 have been amended to further clarify the term as set forth above. Withdrawal of the claim objections is respectfully requested in light of the amendments.

### **Rejection under 35 U.S.C. § 112, second paragraph (Indefiniteness)**

Claims 1, 3-6, 8, 9, 24, and 25 were rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite. More particularly, the Examiner asserted that the recitation of "phosphorylation state-sensitive manner" in the base Claim 1 is unclearly defined. While Applicants believe that the recitation is adequately defined in the specification, Claim 1 has been amended to more clearly describe this recitation as set forth above. With this amendment, Claim 1 now recites, among others, that the binding partner has specificity for the phosphorylatable portion, either (i) only when the phosphorylatable portion is phosphorylated; or (ii) only when the phosphorylatable portion is not phosphorylated. As noted, these amendments are fully supported by the specification as filed. *See* paragraphs [0021] and [0022] of the published application, for example.

As such, Claim 1, and its dependent Claims 3-6, 8, 9, 24, and 25, which were rejected for being dependent from the rejected Claim 1, should now be in compliance with the requirement of 35 U.S.C. 112, second paragraph. Reconsideration of the claims is respectfully requested.

**Rejection under 35 U.S.C. § 112, first paragraph (Written description)**

Claims 1, 3-6, 8, 9, 12-16, 24, and 25 were rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the written description requirement. Regarding these rejections, the Examiner asserted that the claims lack written description because there is no disclosure of a correlation between function and structure of the compound beyond compounds disclosed in the examples in the specification. The Examiner further asserted that the specification lack sufficient variety of species to reflect this variance the genus since the specification does not provide any examples of derivatives. *See* page 9, lines 12-17 of the Office Action. However, for the reasons discussed below, Applicants respectfully submit that an adequate written description for the entire scope of the claimed invention has been provided.

**Necessary and sufficient structures of a substrate polypeptide**

Claim 1 recites a kit that can be used, for example, in assaying protein kinase activity and screening for modulators of protein kinase activity. The claimed kit comprises two or more protein kinase substrate polypeptides, each of which comprises a specificity conferring portion and a phosphorylatable portion. The specificity conferring portion of each substrate polypeptide would be different, but the phosphorylatable portion would be a common sequence of SEQ ID NO: 6 with no residues substituted. In an actual assay or screening, a protein kinase(s) of interest would specifically recognize and phosphorylates a proper substrate polypeptide(s). The degree of phosphorylation of each substrate would be monitored via binding of a specific binding partner to the substrate. Claim 12 further describes the substrate polypeptide, more particularly its specificity conferring portion being a sequence of SEQ ID NO: 2, 5, 8, or 9.

In order for a polypeptide to function as the protein kinase substrate in the presently claimed invention, the sequence would need two requirements, which are a specificity conferring portion and a phosphorylatable portion. As disclosed in the specification, the specificity conferring portion comprises a consensus sequence that would be recognized by a protein kinase, thereby acting as a kinase recognition site. *See* paragraphs [0015] to [0017] and [0034] to [0037] of the published application. The phosphorylatable portion is the 7-amino acid sequence of SEQ ID NO: 6 (i.e. LSFAEPG), which is a common epitope that can be efficiently phosphorylated by many different protein kinases. *See* paragraph [0006] of the published application.

Phosphorylation reaction by a kinase would require at least two steps, the substrate recognition and phosphorylation. As noted, each of the two foregoing portions of the substrate

functions at separate reaction steps of phosphorylation, i.e. recognition and phosphorylation, respectively. Therefore, with the presence of the two portions, the polypeptide would be able to act as the substrate of protein kinases.

The functional sufficiency of the two portions to make the cited substrate was experimentally shown in the Example 1 of the specification. In this example, three different polypeptides, each of which comprised a quite different specificity conferring portion (i.e. "RART", "KKLNRT", and "RRR") and a common phosphorylatable portion (i.e. "LSFAEPG"), were tested for their phosphorylation by a variety of kinases. As readily seen in the Table 1, the tested polypeptides were efficiently phosphorylated by the kinases to at least a degree comparable to the standard substrates. *See*, for example, a maximum activity ( $V_{max}$ ) of each protein kinase to the test polypeptide is about 40% to 220% relative to the  $V_{max}$  of the standard substrates. As described, the tested polypeptides comprise only the above-said two portions. Therefore, the efficient phosphorylation of these polypeptides clearly indicates that the two portions, the specificity conferring portion and phosphorylatable portion, are necessary as well as sufficient for a polypeptide to be the cited protein kinase substrate. Moreover, quite different specificity conferring portions can all be effectively used. Based on these experimental results, one skilled in the art could readily predict that additional, equally different specificity conferring portions could also be effectively employed.

As noted, the present application expressly discloses the functional and structural requirements of a polypeptide to be the claimed protein kinase substrate. As these two requirements provide necessary and sufficient functions and structures of the cited substrate, any polypeptide sequence, which comprises at least the two requirements and further additional amino acids and/or its derivatives, would function as such substrate. Such variance in the substrate polypeptide sequences has already been disclosed throughout the specification as filed, and further would be obvious to a person with ordinary skill in the art.

As such, Claims 1 and 12 and their dependent Claims 4, 5, and 13, which further describe substrate polypeptide sequences comprising additional amino acids, would be in compliance with the written description requirement. Applicants respectfully request the Examiner to reconsider the claims.

As to 3, 6, 8, 9, 14, 16, 24, and 25, through their dependencies, they incorporate all the features of Claim 1 or 12. As mentioned, Claims 1 and 12 are patentable, and therefore their

dependent claims would also be in condition of allowability. Reconsideration of the claims is also requested with respect.

**Allowable subject matter**

Applicants thank the Examiner for indicating that Claims 10 and 11 are allowable.

**No Disclaimers or Disavowals**

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicants are not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicants reserve the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that Applicants have made any disclaimers or disavowals of any subject matter supported by the present application.

**CONCLUSION**

In view of Applicants' foregoing Amendments and Remarks, it is respectfully submitted that the present application is in condition for allowance. Should the Examiner have any remaining concerns which might prevent the prompt allowance of the application, the Examiner is respectfully invited to contact the undersigned at the telephone number appearing below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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